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09/805,681	03/14/2001	Sangita Phadtare	1137-R-00	3645

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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/805,681

Applicant(s)

PHADTARE ET AL.

Examiner

Kathleen M. Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 16 and 18-27 is/are pending in the application.
- 4a) Of the above claim(s) 26 and 27 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 20 is/are allowed.
- 6) ☒ Claim(s) 16, 18, 19 and 21-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Application Status***

1. A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicant's submission filed on March 14, 2005 has been entered.

2. In response to the previous Office action, a Final rejection (mailed on December 10, 2004), Applicants filed an RCE, a response and an amendment received on March 14, 2005. Said amendment cancelled Claim 17, amended Claims 16 and 18-20, and added new Claims 21-27. Thus, Claims 16 and 18-27 are pending in the instant Office action.

### ***Election***

3. The Examiner reiterates that the restriction of record contains three Groups: Group I to proteins, Group II to genes, and Group III to methods of identifying inhibitors of said proteins. Applicant elected to prosecute Group II without traverse in a paper received August 14, 2002.

Newly submitted claims 26-27 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 26 is drawn to previously noted Group III (see written restriction mailed July 22, 2002). Claim 27 is distinct from original Groups I-III (see restriction of record) and is considered new Group IV.

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Group IV is related to original Group I (drawn to proteins) because the gene that encodes the protein is used in the claimed methods. However, these methods are distinct because they neither make nor use the protein. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification (Group I is classified in 530/350 and Group IV is classified in 435/252.3), restriction for examination purposes as indicated is proper.

Groups II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the gene (Group II) can be used for a materially distinct process, such as in hybridization assays to identify novel efflux proteins. Thus, Groups II and IV are patentably distinct. Because these inventions are distinct for the reasons given above and the search required for Group II is not required for Group IV due to the method steps, restriction for examination purposes as indicated is proper. However, possible rejoinder is noted (see below).

Groups III and IV are related as methods of using the DHCP gene. However, these methods are distinct based on their distinct method steps, using different reagents, to produce distinct outcomes. Thus, Groups III and IV are patentably distinct. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification (Group III is classified in 435/6 and Group IV is classified in 435/252.3), restriction for examination purposes as indicated is proper.

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4. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 26-27 are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03. Claims 16 and 18-25 will be examined herein.

*Notice of Possible Rejoinder*

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of M.P.E.P. § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 C.F.R. § 1.116; amendments submitted after allowance are governed by 37 C.F.R. § 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 C.F.R. § 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. § 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Withdrawn process claims that are not commensurate in scope with an allowed product claim

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will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. § 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See M.P.E.P. § 804.01.

#### ***Priority***

6. As previously noted, the instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/228,727 filed on August 29, 2000.

#### ***Drawings***

7. As previously noted, the drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

#### ***Withdrawn - Claim Rejections - 35 U.S.C. § 112***

8. Previous rejection of Claim 20 under 35 U.S.C. § 112, first paragraph, enabling deposit, is withdrawn by virtue of Applicant's amendment to the specification to include proper deposit information as well as Applicant's statement for the record about the availability of said deposit.

***Maintained - Claim Rejections - 35 U.S.C. § 112***

9. Previous rejection of Claims 16, 18, and 19 under 35 U.S.C. § 112, second paragraph, as being indefinite for disrupted genes and gene names is maintained and amended herein. Firstly, considering the clarity of gene disruption, for Claim 16, disruption of *purR* from *E. coli* by *MluI* is clear by virtue of Figure 3 depicting how the use of *MluI* would remove of piece of *purR* form the *E. coli* gene (see plasmid pSP002). However, Claim 16 is not limited to *purR* from *E. coli*. Do all *purR* genes have these *MluI* sites so that deletion of a portion of the gene is clear using the *MluI* restriction enzyme? For the disruption of *ydhB* by *NruI* *or* *Eco47III* is unclear since, if considering Figure 3, the disruption uses both enzymes to remove a *NruI/Eco47III* fragment. Moreover, just as with the disruption of *purR*, if not disrupting *E. coli ydhB*, the use of *NruI* and *Eco47III* is unclear.

Additionally, the instant rejection is maintained, as previously noted, for

“what is the nature of “a *pur* gene”, “a *ydhC* gene”, and “a *ydhB* gene”? Only a single example of each gene from *E. coli* is taught in the instant specification. Must these genes encode something specific? Their identity is particularly unclear with random names like *ydhC* - such naming often occurs in genome sequencing when function cannot be assigned. If a gene is “named” something else, and it is disrupted, would it read on the claim? Clarification is required.” (see previous Office action)

Applicant argues

“With respect to all three terms, a claim term is definite if one skilled in the art would understand the scope of the claim when read in light of the specification. *Union Pacific Resources Co. v. Chesapeake Engineering Corp.*, 57 USPQ2d 1293 (Fed Cir 2001). The specification clearly describes the genes in question at page 11, lines 21-25. *PurR* encodes purine synthesis repressor. *YdhB* encodes a homologue of the *cyn* operon transcriptional activator. The *ydhC* gene encodes a homologue of bicylcomycin [sic]. As such, the applicants respectfully submit that one skilled in the art would understand the nature of these genes in light of the specification.”

The Examiner disagrees that the definition of the terms are clear while read in light of the specification. Firstly, the Examiner notes that limitations from the specification cannot be read into the claims. Moreover, this citation in the specification is not one of definition but of description that in no way includes limitations. The Examiner points expressed previously and reiterated above render the noted terms unclear as to their metes and bounds. Clarification is required.

10. Previous rejection of Claims 16 and 18-19 under 35 U.S.C. § 112, first paragraph, new matter, is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that the disclosure full envisions the claimed genus but Applicant fails to supply any support (i.e., page and line number) to demonstrate said support. As previously noted,

“The specification contains species of Claim 16 in the form of pSP002, pSP006, and pSP007 (depending on the definition of “disrupted”); however, the genus of Claim 16 is not envisioned...

The specification contains species of Claim 18 in the form of pSP003, pSP006, and pSP007 (depending on the definition of “disrupted”); however, the genus of Claim 18 is not envisioned.

The specification contains a species of Claim 19 in the form of pSP007; however, the genus of Claim 19 is not envisioned.”

For the genus of Claim 16, for example, to be envisioned, the full scope of the claimed subject matter must be considered part of the invention. In the instant case, an example of a species of Claim 16 is described in the form of plasmid pSP002; however, the breadth claimed is not described in the specification as originally filed. The same is true for Claims 18 and 19.

Applicant must cite clear support for the claimed genus of Claim 16, Claim 18, and Claim 19 to overcome the instant rejection.



***Withdrawn - Claim Rejections - 35 U.S.C. § 103***

11. Previous rejection of Claim 19 under 35 U.S.C. § 103(a) as being unpatentable over Blattner *et al.* (Science, 1997) in view of Weickert *et al.* is withdrawn as it was presented in the previous Office action. Applicant's arguments are persuasive in that the rejection did not describe how Blattner *et al.* teach DNA encoding dep (SEQ ID NO:3) but how Blattner *et al.* teach DNA encoding SEQ ID NO:2, which is actually *ydhC* (not dep). The previous rejection is, therefore, withdrawn. Moreover, the Examiner agrees that the amendment to the specification to remove the reference that dep is SEQ ID NO:2 from the description of the figures is clearly an error that would have been readily apparent to the skilled artisan and, thus, not new matter. Despite the instant rejection being withdrawn, a similar rejection is set forth below under New Issues. Thus, Applicant's arguments are addressed below.

***Response to Arguments***

12. The following is in response to Applicant's arguments concerning the prior art rejection. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that a plasmid containing the entire dep ORF (encoding SEQ ID NO:3) is not inherently a part of the disclosure of Blattner *et al.* due to the sequencing method used (the Janus strategy as described in Burland *et al.*, 1993). The Examiner finds this argument convincing in that no new rejection under 35 U.S.C. § 102 (b) will be set forth against new Claim 21. However, this argument is not convincing to overcome the rejection under 35 U.S.C. § 103(a) for Claim 19 (which is set forth as a new rejection below considering the change in the specification in the description of the dep gene). As a part of this 103 rejection, the disclosed open reading frame must be expressed independently of the other open reading frames;

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in other words, an expression plasmid of dep alone is rendered obvious (see new rejection of Claim 21 below as well as a rejection analogous to that previously applied to Claim 19).

Applicant further argues the 103-art rejection in that the combination of references renders the plasmid “obvious to try.” In response, the Examiner notes that while a method of identifying the activity of the “putative transport protein” (see GenBank Accession Number AE000261, gene b1657 and AAC74729, encoded protein sequence) can be considered “obvious to try” since such an activity is only postulated, the production of the plasmid is obvious and clearly enabled by the art since the ability to insert a known open reading frame into a multicopy plasmid is well within the skilled artisan’s reach and Blattner *et al.* motivates the skilled artisan to do so. The activities that would be produced when the open reading frame b1657 of Blattner *et al.* is accomplished are inherent; the actual activity of the b1657 open reading frame is not required to motivate the skilled artisan so long as the motivating reason is valid.

Contrary to Applicant’s assertion, the skilled artisan *would* have a reasonable expectation of success that the plasmid can be made with the information provided by Blattner *et al.* and the knowledge of the skilled artisan concerning expression plasmid construction.

Applicant further argues that the decision in *Ex Parte Obukowicz* renders the Examiner’s position untenable; the Examiner disagrees. Particularly, to maintain the 103 rejection of the above Appeal, the Examiner would have had to motivate the practice of a method. That is not the case here. Only the production of a plasmid be motivated, and that has clearly been set forth in prosecution. Producing multicopy plasmid is *not* a new technology. Perhaps the use of said plasmids may be; but that is not at issue here.

**NEW ISSUES*****Claim Objections***

13. Applicant is advised that should claim 23 be found allowable, claims 24 and 25 will be objected to under 37 C.F.R. § 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See M.P.E.P. § 706.03(k). For Claim 24, the limitation of being “derived from *E. coli*” in no way limits the nucleic acid molecule that must already encode an *E. coli* protein since “derived from” is not defined in the specification as having some particular requirements. Moreover, for Claim 25, the activity of the encoded protein is inherent and is the only additional limitation for this claim.

***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 25 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “functionally equivalent compound” with respect to DHCP is unclear. What function of DHCP must be possessed by said compound? Its ability to be effluxed by SEQ ID NO:3? Its antibacterial activity and if so, what portion of the molecule garners said activity? Clarification is required.

***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 23-25 are rejected under 35 U.S.C. § 102(b) as being anticipated by Blattner *et al.* as evidenced by GenBank Accession Number AE000261. The instant claims are drawn to a, isolated nucleic acid molecule that encodes SEQ ID NO:3.

Blattner *et al.* teach a 11033 base pair linear DNA molecule as described in GenBank Accession Number AE000261, which contains sequence from 837-2006 whose complement encodes “b1657”, which protein is described as a “putative transport protein”. This portion of the sequence exactly encodes SEQ ID NO:3.

Applicant’s arguments concerning Blattner *et al.* not teaching the entire open reading frame on the same plasmid are not valid against the instant rejection because while Blattner *et al.* may not have reduced the isolated DNA of the GenBank Accession number to practice per se, the genus of Claims 23-25 is clearly taught by the prior art since the GenBank Accession number describes a 11033 base pair linear DNA.

***Claim Rejections - 35 U.S.C. § 103***

16. Claims 19, 21, and 22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Blattner *et al.* (Science, 1997) in view of Weickert *et al.* The instant claims are drawn to

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multicopy plasmids containing the *dep* gene from *E. coli* and not containing particular other genes.

Blattner *et al.* teach a 11033 base pair linear DNA molecule as described in GenBank Accession Number AE000261, which contains sequence from 837-2006 whose complement encodes “b1657”, which protein is described as a “putative transport protein”. This portion of the sequence exactly encodes SEQ ID NO:3. This DNA also has the inherent property of encoding a protein conferring DHCP resistance when present in multiple copies. The Examiner notes that on page 10 of the instant specification, the GenBank reference noted above is admitted as prior art. While Blattner *et al.* teach sequencing techniques using plasmids, no expression plasmids are taught for the individual open reading frames as disclosed.

Weickert *et al.* teach the heterologous expression of proteins in *E. coli* using multicopy plasmids to achieve good protein production (see Table 1, page 495).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Blattner *et al.* and Weickert *et al.* to make multicopy plasmids for expression of the open reading frames disclosed by Blattner *et al.* in bacterial host cells because Blattner *et al.* specifically suggest “analysis of biochemical and catalytic properties of the expressed proteins” (see page 1461, left column) and Weickert *et al.* specifically teach multicopy plasmids as a technique for optimizing heterologous protein overproduction, which overproduction is required for protein purification and activity assays. One would have been motivated to combine the above teachings to overproduce the encoded protein, which Blattner *et al.* describe as a putative transport membrane protein, to attribute a specific function to the protein – a common practice in the art.

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***Summary of Pending Issues***

17. The following is a summary of the issues pending in the instant application:
- a) Claims 16, 18, and 19 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for disrupted genes and gene names.
  - b) Claims 16 and 18-19 stand rejected under 35 U.S.C. § 112, first paragraph, new matter, is maintained.
  - c) Claims 24-25 are provisionally objected to as duplicate claims of Claim 23.
  - d) Claim 25 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "functionally equivalent compound" with respect to DHCP.
  - e) Claims 23-25 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Blattner et al. as evidenced by GenBank Accession Number AE000261.
  - f) Claims 19, 21, and 22 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Blattner et al. in view of Weickert et al.

***Conclusion***

18. Claims 16 and 18, 19, and 21-25 are not allowed for the reasons identified in the numbered sections of this Office action; Claim 20 is allowed. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M. Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr  
Primary Examiner  
Art Unit 1652



June 7, 2005